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10/015,389	12/11/2001	Kevin P. Baker	GNE.2830P1C48	9880

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EXAMINER	
KAPUST, RACHEL B	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,389	BAKER ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33,37 and 41-47* is/are rejected.

7)☒ Claim(s) *34-36 and 38-40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

According to the priority statement of September 9, 2002, the claimed subject matter defined in the instant application is supported by parent application serial nos. 60/100848, 09/403297, 09/946374, PCT/US99/20111, and PCT/US00/04342. Based on the information given by applicant and an inspection of the patent applications, the examiner has concluded that the subject matter defined in this application is supported by the disclosure in application serial no. PCT/US00/04342, filed February 18, 2000 but is not supported by any of the earlier applications because no utility for the claimed polynucleotide, PRO 1412, is disclosed in the earlier applications. The results of the chondrocyte proliferation assay and the fetal hemoglobin induction in erythroblastic cell line assays are first reported in PCT/US00/04342. Accordingly, the subject matter defined in claims 28-47 has an effective filing date of February 18, 2000.

Should the Applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to February 18, 2000 that specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled prior to February 18, 2000.

Claim Objections

Claim 38 is objected to because of the following informalities: there are two claim 38's. One of them needs to be canceled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28-33, 37, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation that the encoded polypeptide comprises an "extracellular domain"..."lacking its associated signal peptide" (claim 28, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of maturation.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as indefinite in the limitation "stringent conditions". Stringent conditions are not defined in the specification; only examples of conditions are presented on p. 306. Thus, one of skill in the art would not know what conditions, and thus what molecules, Applicant intended the claims to encompass.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-32 and 44-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide having at least 80% nucleotide sequence identity to the polynucleotide encoding SEQ ID NO: 139 or the nucleic acid encoding the mature form of the polypeptide, which polypeptide induces proliferation of chondrocytes, does not reasonably provide enablement for a polynucleotide encoding a polypeptide not identical to at least the mature form of SEQ ID NO: 140 which does not have this activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a polynucleotide having at least 80% nucleotide sequence identity to the polynucleotides encoding a polypeptide SEQ ID NO: 140 or the extracellular domain thereof, both referred to as PRO1412, and polynucleotides identified by hybridization to these polynucleotides. There is no functional limitation in the claims. Applicants have taught the polynucleotide encoding the polypeptide of SEQ ID NO: 140, as well as the putative signal sequence. This polypeptide was shown to have chondrocyte proliferation activity (p. 514, Assay #111), but Applicant does not indicate whether the entire protein or an extracellular region was used. This polypeptide was also shown to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line (p. 511, Assay #107).

The claims encompass an unreasonable number of inoperative polynucleotides, which the skilled artisan would not know how to use. While the specification suggests that the polypeptide of SEQ ID NO: 140 is a transmembrane protein (p. 117), it provides no other teachings as to the structural and related functional characteristics of this protein. As opposed to the claims, what is disclosed about PRO1412 is narrow: a single polypeptide with one disclosed function and no other obvious specific functions. Further, it is not clear from the disclosure whether the extracellular region alone, the entire molecule, or both, have this function. Knowledge of one molecule's structure and function does not provide predictability about function of a structurally related molecule, even within the same class.

There are no working examples of polypeptides less than 100% identical to the polypeptide comprising SEQ ID NO: 140. The skilled artisan would not know how to use non-identical polypeptides or polynucleotides encoding them on the basis of teachings in the prior art or specification unless they possessed the chondrocyte proliferation activity or the fetal hemoglobin induction activity disclosed in the instant specification. The specification does not provide guidance for using polypeptides related to (*i.e.*, 80%-99% identity) but not identical to

SEQ ID NO: 140 which do not have the single specific disclosed activity shown for PRO1412. The claims are broad because they do not require the claimed polynucleotide to be identical to the disclosed sequence and because the claims have no functional limitation.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of transmembrane proteins, and lack of knowledge about function(s) of encompassed polynucleotides encoding polypeptides structurally related to SEQ ID NO: 140, the two limited working examples of the PRO1412 polypeptide and its two functions, the lack of direction or guidance for using polypeptides that are not identical to at least the mature form of SEQ ID NO: 140, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 28-32 and 44-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides encoding polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the encoded polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the protein has the disclosed activity. Accordingly, in the

absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides encoding polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 140 but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to polynucleotides polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, the polynucleotides being at least

10 nucleotides in length. The claims do not require that the encoded polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. As stated above, it is not even clear what region of the protein has the disclosed activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides encoding polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 140 but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 28-32 and 41-47 are rejected under 35 U.S.C. 102(a) as being anticipated by International Patent Application Publication No. WO 00/00610 (Lal *et al.*, publication date January 6, 2000). These claims encompass polynucleotides that are at least 80%, 85%, 90%, 95%, or 99% identical to the nucleic acid sequence of SEQ ID NO: 139. The claims also encompass nucleic acid sequences that hybridize to SEQ ID NO: 139. WO 00/00610 teaches SEQ ID NO: 158, which is 99% identical to SEQ ID NO: 139 (see attached alignment). Furthermore, SEQ ID NO: 158 encodes a polypeptide comprising SEQ ID NO: 24, which is 99% identical to SEQ ID NO: 140 of the current application (see attached alignment). WO 00/00610 further teaches expression vectors comprising SEQ ID NO: 158, host cells containing the expression vectors, and using *E. coli*, yeast, and mammalian cells as host cells (p. 14, 34).

Allowable Subject Matter

Claims 34-36 and 38-40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CLAIMS 28-33, 37, and 41-47 ARE REJECTED. CLAIMS 34-36 and 38-40 ARE OBJECTED TO.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (703) 305-0634. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm. Please note for your records that as of January 20, 2004, the examiner's new telephone number will be (571) 272-0886.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RBK
1/19/04

JANET ANDRES
PATENT EXAMINER